# ANNEX I SUMMARY OF PRODUCT CHARACTERISTICS

### 1. NAME OF THE MEDICINAL PRODUCT

Rhokiinsa 200 micrograms/ml eye drops, solution.

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution contains 200 micrograms netarsudil (as mesylate).

Excipient(s) with known effect

Each ml of solution contains 150 micrograms benzalkonium chloride.

For the full list of excipients, see section 6.1.

### 3. PHARMACEUTICAL FORM

Eye drops, solution (eye drops).

Clear solution, pH 5 (approximately).

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Rhokiinsa is indicated for the reduction of elevated intraocular pressure (IOP) in adult patients with primary open-angle glaucoma or ocular hypertension.

### 4.2 Posology and method of administration

Treatment with Rhokiinsa should only be initiated by an ophthalmologist or a healthcare professional qualified in ophthalmology.

### Posology

The recommended dose is one drop in the affected eye(s) once daily in the evening. Patients should not instill more than one drop in the affected eye(s) each day.

If one dose is missed, treatment should continue with the next dose in the evening.

# Paediatric population

The safety and efficacy of Rhokiinsa in children below the age of 18 years have not been established. No data are available.

# Method of administration

For ocular use.

No data on potential interactions specific to netarsudil is currently available (see section 4.5). If netarsudil is to be used concomitantly with other topical ophthalmic medicinal products, each medicinal product should be administered at least five (5) minutes apart. Due to netarsudil's vasodilating properties, other eye drops should be administered before. Eye ointments should be administered last.

Contact lenses should be removed prior to instillation of netarsudil and may be reinserted 15 minutes following its administration (see section 4.4).

The tip of the dispensing container should avoid contacting the eye, surrounding structures, fingers, or any other surface in order to avoid contamination of the solution. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

### 4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

# 4.4 Special warnings and precautions for use

### Ocular effects

Twice a day dosing is not well tolerated and is not recommended. Netarsudil dosed twice daily provided slightly larger IOP reductions, but had a less favorable safety profile as reflected in a higher rate and increased severity of ocular adverse reactions. Twice a day dosing was also associated with a higher discontinuation rate due to adverse reactions (53.8%) during a 12-month study. It is therefore recommended to dose netarsudil once daily.

### Reticular epithelial corneal oedema

Reticular epithelial corneal oedema (RECE) has been reported following administration of medicinal products containing netarsudil, particularly in patients with preexisting corneal oedema or prior ocular surgery. RECE typically resolves upon discontinuation of the medicinal product containing netarsudil. Patients should be advised to notify their physician if they experience decreased vision or eye pain while using Rhokiinsa.

The efficacy of netarsudil has not been studied beyond 12 months.

### Excipients with known effect

### Benzalkonium chloride

This medicinal product contains benzalkonium chloride.

Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface and is known to discolour soft contact lenses. It should be used with caution in dry eye patients and in patients where the cornea may be compromised. Patients should be monitored in case of prolonged use.

### 4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

# 4.6 Fertility, pregnancy and lactation

# **Pregnancy**

There are no or limited amount of data from the use of netarsudil in pregnant women. No effects during pregnancy are anticipated, since systemic exposure to netarsudil is negligible (see section 5.2). Animal studies with intravenous administration do not indicate direct or indirect harmful effects with respect to reproductive toxicity at clinically relevant exposures (see section 5.3). Rhokiinsa should not be used during pregnancy unless the clinical condition of the woman requires treatment with netarsudil.

### Breast-feeding

It is unknown whether netarsudil/metabolites are excreted in human milk. However, while no effects on the breastfed newborn/infant are anticipated since the systemic exposure of breast-feeding women to netarsudil is expected to be negligible, no relevant clinical data are available (see section 5.2). A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Rhokiinsa therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

### Fertility

There are no data on the effects of netarsudil on male or female fertility. However, no effects are anticipated, since systemic exposure to netarsudil is negligible (see section 5.2).

# 4.7 Effects on ability to drive and use machines

Rhokiinsa has negligible influence on the ability to drive and use machines. If transient blurred vision occurs at instillation, the patient should wait until the vision clears before driving or using machines.

### 4.8 Undesirable effects

## Summary of the safety profile

The most common adverse reactions observed in the clinical trials were conjunctival hyperemia (51% of patients), cornea verticillata (17%), instillation site pain (17%), conjunctival haemorrhage (8%), instillation site erythema (8%), corneal staining (7%), blurred vision (6%), increased lacrimation (6%) and erythema of eyelid (5%). Serious adverse reactions were not reported in clinical trials.

### Tabulated list of adverse reactions

The following adverse reactions have been reported with netarsudil, dosed once daily. Reactions are classified according to the convention: very common ( $\geq 1/10$ ), common ( $\geq 1/100$  to < 1/100), uncommon ( $\geq 1/1000$ ), rare ( $\geq 1/1000$ ), rare ( $\geq 1/1000$ ), very rare (< 1/10000) or not known (cannot be estimated from the available data).

System organ classification	Frequency	Adverse reactions
Immune system disorders	Uncommon	Hypersensitivity
Nervous system disorders	Common	Headache
	Uncommon	Dizziness
Eye disorders	Very	Conjunctival hyperaemia <sup>1</sup> ,
	common	Cornea verticillata <sup>1</sup> ,
		Instillation site pain
	Common	Conjunctival haemorrhage,
		Vision blurred,
		Lacrimation increased,
		Erythema of eyelid,
		Eye pruritis,
		Eye irritation,
		Visual acuity reduced,
		Eyelid oedema,
		Punctate keratitis,
		Conjunctival oedema,
		Foreign body sensation in eyes,
		Conjunctivitis,
		Conjunctivitis allergic,
		Photophobia,
		Eyelid pruritus,
		Eye pain,

System organ classification	Frequency	Adverse reactions
		Corneal opacity,
		Dry eye,
		Eye discharge,
		Instillation site erythema,
		Instillation site discomfort,
		Instillation site pruritis,
		Vital dye staining cornea present,
		Intraocular pressure increased
	Uncommon	Ocular hyperaemia,
		Blepharitis,
		Corneal disorder,
		Eyelid margin crusting,
		Eye allergy,
		Conjunctival follicles,
		Ocular discomfort,
		Eye swelling, Corneal deposits,
		Eyelid disorder,
		Meibomian gland dysfuntion,
		Corneal pigmentation,
		Diplopia,
		Ectropion,
		Lenticular opacities,
		Noninfective conjunctivitis,
		Abnormal sensation in the eye,
		Asthenopia,
		Episcleral hyperaemia,
		Halo vision,
		Keratitis,
		Refraction disorder,
		Anterior chamber flare,
		Anterior chamber inflammation,
		Blindness,
		Conjunctival irritation,
		Conjunctivochalasis,
		Diabetic retinopathy,
		Eczema eyelids,
		Eyelid skin dryness,
		Glaucoma,
		Growth of eyelashes,
		Iris adhesions,
		Iris bombe, Iritis,
		Ocular hypertension,
		Visual impairment,
		Corneal dystrophy,
		Instillation site foreign body sensation,
		Instillation site irritation,
		Glassy eyes,
		Fatigue,
		Instillation site dryness,
		Instillation site oedema,
		Instillation site paraesthesia,
		Conjunctival staining,
		Optic nerve cup/disc ratio increased,
		Madarosis
		Visual field defect
	Not known	Reticular epithelial corneal oedema <sup>2</sup>
Respiratory, thoracic and mediastinal disorders	Uncommon	Nasal discomfort,
		Rhinalgia
Skin and subcutaneous tissue disorders	Uncommon	Dermatitis allergic,
	1	Dermatitis contact,

System organ classification	Frequency	Adverse reactions
		Lichenification,
		Petechiae
Musculoskeletal and connective tissue disorders	Uncommon	Polychondritis
Injury, poisoning and procedural complications	Uncommon	Excoriation

<sup>&</sup>lt;sup>1</sup> See Description of selected adverse reactions for further information

# Description of selected adverse reactions

### Conjunctival hyperaemia

Conjunctival hyperaemia was the most frequently reported adverse reaction associated with netarsudil treatment in clinical trials and it is attributed to the vasodilation effect of the Rho kinase inhibitor drug class. Conjunctival hyperaemia was typically mild in severity and sporadic. However, there was a relatively small proportion of subjects with moderate or severe hyperaemia who discontinued treatment because of this adverse reaction (6.0% in Phase 3 clinical trials).

### Cornea verticillata

Cornea verticillata occurred in approximately 20% of the patients in controlled Phase 3 clinical trials. The cornea verticillata seen in netarsudil-treated patients were first noted at 4 weeks of daily dosing. This reaction did not result in any apparent visual functional changes in patients. The majority of cornea verticillata resolved upon discontinuation of treatment. The incidence of cornea verticillata was higher in certain subpopulations: elderly (≥65 years) versus non-elderly (24.8 vs. 15.9%); males versus females (24.4 vs. 18.4%) and in white versus other races (25.6 vs. 7.0%).

### Special populations

### Elderly subjects

With the exception of cornea verticillata (see above), no difference in the safety profile for Rhokiinsa has been observed between subjects aged <65 or ≥65 years.

### Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

### 4.9 Overdose

Systemic exposure to netarsudil following topical ocular administration has been shown to be negligible. If topical overdose of netarsudil should occur, the eye(s) may be flushed with tap water. Treatment of an overdose would include supportive and symptomatic therapy.

### 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals, antiglaucoma preparations and miotics, ATC code: S01EX05

# Mechanism of action

Netarsudil, a Rho kinase inhibitor, is believed to reduce IOP by increasing outflow of aqueous humor. Studies in animal and man suggest that the main mechanism of action is increased trabecular outflow. These studies also suggest that netarsudil lowers IOP by reducing episcleral venous pressure.

<sup>&</sup>lt;sup>2</sup> Additional adverse reaction observed with netarsudil monotherapy

### Clinical efficacy and safety

A randomised, double-blind, multicentre Phase 3 clinical trial compared the efficacy and safety of netarsudil once daily with that of timolol maleate 0.5% twice daily in reducing IOP in a total of 708 patients with open-angle glaucoma or ocular hypertension. The median age of study participants was 65.5 years (range 18 to 91 years).

The study was designed to show non-inferiority of netarsudil when dosed once daily in the evening to timolol maleate 0.5% dosed twice daily in patients with a baseline IOP of >20 mmHg and <25 mmHg. The primary efficacy outcome measure was mean IOP at each of 9 timepoints measured at 08:00, 10:00 and 16:00 on day 15, day 43 and day 90. The non-inferiority margin applied was a difference in mean IOP  $\leq$ 1.5 mmHg for all time points over all visits through 3 months and  $\leq$ 1.0 mmHg at a majority of these time points. The IOP reduction with netarsudil dosed once daily was non-inferior to the effect of timolol 0.5% dosed twice daily in patients with baseline IOP of  $\leq$ 25 mmHg (Table 1). Efficacy was also investigated in patients with baseline IOP  $\geq$ 25 mmHg and  $\leq$ 30 mmHg. Netarsudil demonstrated clinically relevant reductions in IOP at all timepoints, however non-inferiority to timolol was not demonstrated in this population with baseline IOP  $\geq$ 25 mmHg and  $\leq$ 30 mmHg (Table 2).

Table 1: Mean IOP by visit: PP population with baseline IOP <25 mmHg

Study visit and time point		Netarsudil 0.02% Once daily		Timolol 0.5% twice daily		<u>Difference (95% CI)</u> Netarsudil – Timolol
•		N	IOP	N	IOP	
Baseline	08:00	186	22.40	186	22.44	
	10:00	186	21.06	186	21.27	
	16:00	186	20.69	186	20.69	
Day 15	08:00	184	17.68	183	17.51	0.17 (-0.43, 0.77)
	10:00	181	16.55	183	16.71	-0.16 (-0.73, 0.41)
	16:00	181	16.32	183	16.92	-0.60 (-1.16, -0.04)
Day 43	08:00	177	17.84	183	17.60	0.25 (-0.34, 0.83)
	10:00	177	16.75	182	16.98	-0.22 (-0.82, 0.37)
	16:00	176	16.57	182	16.67	-0.10 (-0.66, 0.46)
Day 90	08:00	167	17.86	179	17.29	0.56 (-0.02, 1.15)
	10:00	166	16.90	179	16.69	0.21 (-0.37, 0.79)
	16:00	165	16.73	179	16.80	-0.07 (-0.68, 0.55)

Table 2: Mean IOP by visit: PP population with baseline IOP ≥25 and <30 mmHg

Study visit and time point		Netarsud	udil 0.02% Timolo		% twice daily	Difference (95% CI)
		Once daily				Netarsudil - Timolol
		N	IOP	N	IOP	
Baseline	08:00	120	26.30	130	25.96	
	10:00	120	25.18	130	24.91	
	16:00	120	24.48	130	23.99	
Day 15	08:00	118	21.57	129	20.15	1.42 (0.51, 2.34)
	10:00	116	20.09	129	19.34	0.75 (-0.15, 1.64)
	16:00	116	20.01	129	19.17	0.83 (0.00, 1.67)
Day 43	08:00	112	21.99	127	19.84	2.14 (1.16, 3.13)
	10:00	109	20.33	127	19.19	1.15 (0.30, 1.99)
	16:00	109	20.03	127	19.63	0.41 (-0.47, 1.29)
Day 90	08:00	94	21.71	121	19.91	1.79 (0.74, 2.85)
	10:00	93	20.80	120	18.95	1.85 (0.89, 2.81)
	16:00	93	20.31	120	18.94	1.37 (0.46, 2.28)

The safety of netarsudil has been evaluated in clinical trials, including four well-controlled Phase 3 studies.

Approximately 75% of subjects included in the netarsudil treatment groups of Phase 3 studies were Caucasian and 24% Black or African American. Over half were aged  $\geq$  65 years. With the exception of the incidence of cornea verticillata, no other difference in safety profile was observed between races or age groups (see section 4.8).

Completion rates in Phase 3 studies were lower in the netarsudil treatment group when compared with the timolol maleate group. Subjects with known contraindications or hypersensitivity to timolol were excluded from the studies. Discontinuation rates due to adverse reactions were 19.3% for the netarsudil treatment group versus 1.7% for the timolol maleate group. The majority of discontinuations in the netarsudil group were associated with ocular adverse reactions, whereas the majority of discontinuations in the timolol group were associated with non-ocular adverse reactions. The most frequently reported adverse reactions associated with discontinuation in the Rhokiinsa groups were conjunctival hyperemia (5.8%), cornea verticillata (3.7%) and vision blurred (1.4%). The incidences of hyperemia and vision blurred were sporadic in nature.

The efficacy and safety of netarsudil in subjects with compromised corneal epithelium or co-existing ocular pathologies e.g. pseudoexfoliation and dispersion pigment syndrome has not been established.

### Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Rhokiinsa in all subsets of the paediatric population for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension. (see section 4.2 for information on paediatric use).

# **5.2** Pharmacokinetic properties

# **Absorption**

The systemic exposures of netarsudil and its active metabolite, AR-13503, were evaluated in 18 healthy subjects after topical ocular administration of netarsudil once daily (one drop bilaterally in the morning) for 8 days. There were no quantifiable plasma concentrations of netarsudil (lower limit of quantitation (LLOQ) 0.100 ng/ml) post dose on day 1 and day 8. Only one plasma concentration at 0.11 ng/ml for the active metabolite was observed for one subject on day 8 at 8 hours post-dose.

### Biotransformation

After topical ocular dosing, netarsudil is metabolised by esterases in the eye to an active metabolite, AR-13503.

# 5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to development. Effects in non-clinical trials were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

Intravenous administration of netarsudil mesylate to pregnant rats and rabbits during organogenesis did not produce adverse embryofetal effects at clinically relevant systemic exposures. In pregnant rats, 0.3 mg/kg/day (1 000 times the recommended ophthalmic dose) and higher showed increased post-implantation loss and reduced foetal viability. In pregnant rabbits, 3 mg/kg/day (10 000 times the recommended ophthalmic dose) and higher showed an increase in post-implantation loss and a decrease in foetal weight.

Long-term studies in animals have not been performed to evaluate the carcinogenic potential of netarsudil.

Netarsudil was not mutagenic in a bacterial mutation assay, in a mouse lymphoma assay, or in a rat micronucleus test.

Netarsudil and its active metabolite AR-13503 was found to have a possible phototoxic potential in a modified 3T3 NRU-PT in vitro assay, where the wavelength was extended to include UVB light.

### 6. PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Benzalkonium chloride Mannitol Boric acid Sodium hydroxide (for pH-adjustment) Water for injections

# 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

3 years.

Opened bottle: 4 weeks after first opening the bottle. Do not store above 25°C.

## 6.4 Special precautions for storage

Store in a refrigerator  $(2^{\circ}C - 8^{\circ}C)$  until opened.

For storage conditions after first opening of the medicinal product, see section 6.3.

### 6.5 Nature and contents of container

Rhokiinsa is supplied sterile in opaque white low density polyethylene bottles (2.5 ml fill in a 4 ml container) and tips with white polypropylene caps and anti-tamper seals.

Carton containing 1 bottle.

### 6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

# 7. MARKETING AUTHORISATION HOLDER

Santen Oy Niittyhaankatu 20 33720 Tampere Finland

# 8. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1400/001

# 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19/11/2019 Date of latest renewal: 06/09/2024

# 10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency <a href="https://www.ema.europa.eu">https://www.ema.europa.eu</a>.

## **ANNEX II**

- A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

### A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

Santen Oy Kelloportinkatu 1 33100 Tampere Finland

### B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

# C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

• Periodic safety update reports (PSURs)

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

# D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

• Risk management plan (RMP)

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

# ANNEX III LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON OUTER PACKAGING
OUTER CARTON
1. NAME OF THE MEDICINAL PRODUCT
1. NAME OF THE MEDICINAL PRODUCT
Rhokiinsa 200 micrograms/ml eye drops, solution netarsudil
2. STATEMENT OF ACTIVE SUBSTANCE(S)
1 ml of solution contains 200 micrograms netarsudil (as mesylate).
3. LIST OF EXCIPIENTS
Benzalkonium chloride, boric acid, mannitol, sodium hydroxide, water for injections. Read the package leaflet before use.
4. PHARMACEUTICAL FORM AND CONTENTS
Eye drops, solution 1 x 2.5 ml
5. METHOD AND ROUTE(S) OF ADMINISTRATION
Read the package leaflet before use. Ocular use.
6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN
Keep out of the sight and reach of children.
7. OTHER SPECIAL WARNING(S), IF NECESSARY
8. EXPIRY DATE
EXP Discard 4 weeks after first opening. Open date:  9. SPECIAL STORAGE CONDITIONS
7. STECKE STORIGE COMPITIONS

Store in a refrigerator until opened. Once opened, do not store above 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS
OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF
APPROPRIATE
11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER
Santen Oy Niittyhaankatu 20 33720 Tampere Finland
12. MARKETING AUTHORISATION NUMBER(S)
EU/1/19/1400/001
13. BATCH NUMBER
Lot
14. GENERAL CLASSIFICATION FOR SUPPLY
15. INSTRUCTIONS ON USE
16. INFORMATION IN BRAILLE
Rhokiinsa
17. UNIQUE IDENTIFIER – 2D BARCODE
2D barcode carrying the unique identifier included.
18. UNIQUE IDENTIFIER - HUMAN READABLE DATA
PC SN NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS				
BOTTLE LABEL				
1.	NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION			
Rhok netars Ocula				
2.	METHOD OF ADMINISTRATION			
3.	EXPIRY DATE			
EXP				
4.	BATCH NUMBER			
Lot				
5.	CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT			
2.5 m	1			
6.	OTHER			

B. PACKAGE LEAFLET

### Package leaflet: Information for the patient

# Rhokiinsa 200 micrograms/ml eye drops, solution netarsudil

# Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

### What is in this leaflet

- 1. What Rhokiinsa is and what it is used for
- 2. What you need to know before you use Rhokiinsa
- 3. How to use Rhokiinsa
- 4. Possible side effects
- 5. How to store Rhokiinsa
- 6. Contents of the pack and other information

### 1. What Rhokiinsa is and what it is used for

Rhokiinsa contains an active substance called netarsudil. Netarsudil belongs to a group of medicines called "Rho kinase inhibitors", which work to reduce the amount of fluid inside the eye and so lower its pressure.

Rhokiinsa is used to lower pressure in the eyes in adults who have an eye condition known as glaucoma or who have raised pressure in their eyes. If the pressure in the eye is too high, it can damage your sight.

### 2. What you need to know before you use Rhokiinsa

### Do not use Rhokiinsa:

- if you are allergic to netarsudil or any of the other ingredients of this medicine (listed in section 6).

# Warnings and precautions

- Do not use Rhokiinsa more than once a day, as you may experience more side effects.
- Tell your doctor if you experience decreased vision or eye pain during treatment with this medicine. This might be due to a type of swelling of the clear outer layer of the eye (reticular epithelial corneal oedema). This effect has been reported following administration of this medicine to the eye in patients with certain risk factors, including previous surgery to the eye. It usually improves following discontinuation of the medicine.

### Children and adolescents

Rhokiinsa should not be used in children and teenagers under 18 years of age as it has only been studied in adults.

### Other medicines and Rhokiinsa

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines (see section 3 'How to use Rhokiinsa').

### **Pregnancy and breast-feeding**

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. Do not use Rhokiinsa if you are pregnant or breastfeeding unless your doctor still recommends it.

### **Driving and using machines**

Rhokiinsa has negligible influence on the ability to drive and use machines. You may find that your vision is blurred or abnormal just after using Rhokiinsa. Do not drive or use machines until the symptoms are cleared.

### Rhokiinsa contains benzalkonium chloride

This medicine contains approximately 150 micrograms benzalkonium chloride in each ml of solution.

Benzalkonium chloride may be absorbed by soft contact lenses and may change the colour of the contact lenses. You should remove contact lenses before using this medicine and put them back 15 minutes afterwards (see section 3 'How to use Rhokiinsa').

Benzalkonium chloride may also cause eye irritation, especially if you have dry eyes or disorders of the cornea (the clear layer at the front of the eye). If you feel abnormal eye sensation, stinging or pain in the eye after using this medicine, talk to your doctor.

### 3. How to use Rhokiinsa

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Only use Rhokiinsa for your eyes (ocular use). Do not swallow or inject.

The recommended dose is one drop in the affected eye or eyes once a day in the evening. Use the medicine at around the same time each day.

Do not use more than one drop in the affected eye(s) once a day.

### How to use



- Wash your hands before you start. Contact lenses should be removed prior to instillation of Rhokiinsa (see section 2 'Rhokiinsa contains benzalkonium chloride').
- Do not touch the dropper with your fingers when opening or closing the bottle. It could contaminate the drops.
- Twist off the bottle cap, and lie the cap on a clean surface on its side. Continue to hold the bottle, ensuring that the tip doesn't come into contact with anything.
- Hold the bottle, pointing down, between your thumb and fingers.
- Tilt your head back.
- Pull down your lower eyelid with a clean finger to form a 'pocket' between the eyelid and your eye. The drop will go in here (Picture 1).

- Bring the bottle tip close to the eye. Do this in front of a mirror if it helps.
- Do not touch your eye, eyelid, surrounding areas or other surfaces with the dropper. It could contaminate the drops.
- Gently squeeze the bottle to release one drop of Rhokiinsa into your eye.
- Only put one drop into your eye each time. If a drop misses your eye, try again.
- If you need to use the drops in both eyes, repeat the steps for your other eye while you have the bottle open.
- Put back the bottle cap to close the bottle.

If you are using other eye drops, wait at least five minutes after using them and then use Rhokiinsa last due to netarsudil's vasodilating properties. If you are using eye ointments, these should be used last.

# If you use more Rhokiinsa than you should

Rinse your eye with warm water. Do not put in any more drops until it is time for your next regular dose.

# If you forget to use Rhokiinsa

Continue with the next dose as planned. Do not use a double dose to make up for a forgotten dose.

# If you stop using Rhokiinsa

Do not stop using Rhokiinsa without first speaking to your doctor. If you stop using Rhokiinsa the pressure in your eye will not be controlled which could lead to loss of sight.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

### 4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following non-serious side effects have been observed with Rhokiinsa:

**Very common** side effects (may affect more than 1 in 10 people)

• Effects in the eye:

Eye redness; fine deposits on the front of the eye (corneal verticillata)

Pain where the drops have been put in

# **Common** side effects (may affect up to 1 in 10 people)

• Effects in the eye:

Infection or inflammation of the eye, dryness of the eye or small breaks in the film of liquid on the surface of the eye (conjunctivitis, punctate keratitis); eye inflammation caused by an allergic reaction or prominent blood vessels;

Eye discharge; eyes can become watery;

Eye pain; feeling of grittiness or having something in the eye; general eye redness shortly after drops are put in; spots or patches of eye redness;

Itchy eyelids; swelling around the eye;

Clouding of the eye and vision may decrease somewhat; sensitive to light; blurred vision

• General side effects: Headache

### **Uncommon** side effects (may affect up to 1 in 100 people)

• Effects in the eye:

Increased fluid pressure inside the eye;

Inflammation of the coloured part of the eye (the iris); bulging of iris; small colored spots on the eye surface;

Growth of eyelashes; loss of eyelashes (madarosis);

Eyelid dryness; abnormal turning outward of the lower eyelid; eye dryness caused by inflammation of the glands of the eyelids; eyelid crusting;

Eye disease related to diabetes; (diabetic retinopathy);

Excess folds of the conjunctiva (conjunctivochalasis);

Blindness; blurred, double and halo vision; cataracts;

Eye allergy;

Glassy eyes; tiredness

• General side effects:

Increased allergic symptoms;

Dizziness;

Nasal discomfort and pain;

• Effects on the skin: redness or itching of the skin; rash on skin; inflammation of the cartilage; picking of the skin

Not known side effects (cannot be estimated from the available data)

• Effects in the eye:

Swelling of the clear outer layer of the eye (reticular epithelial corneal oedema)

### Reporting of side effects

If you get any side effects, talk to your doctor, or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in <u>Appendix V</u>. By reporting side effects you can help provide more information on the safety of this medicine.

### 5. How to store Rhokiinsa

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and bottle label after "EXP". The expiry date refers to the last day of that month.

Unopened bottles: Store in a refrigerator (2°C - 8°C).

After opening the bottle: Do not store above 25°C.

Do not use the bottle 4 weeks after first opening to prevent infections and use a new bottle.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

### 6. Contents of the pack and other information

### What Rhokiinsa contains

- The active substance is netarsudil. Each ml of solution contains 200 micrograms netarsudil (as mesylate).
- The other excipients are benzalkonium chloride (see section 2 under 'Rhokiinsa contains benzalkonium chloride'), mannitol, boric acid, sodium hydroxide (for pH adjustment) and water for injections.

## What Rhokiinsa looks like and contents of the pack

Rhokiinsa 200 micrograms/ml eye drops, solution (eye drops) is a clear, liquid eye drop solution in a plastic bottle. Each bottle contains 2.5 ml of the medicine and each pack contains one bottle with a screw-cap.

### **Marketing Authorisation Holder**

Santen Oy Niittyhaankatu 20, 33720 Tampere, Finland

### Manufacturer

Santen Oy, Kelloportinkatu 1, 33100 Tampere, Finland

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

### België/Belgique/Belgien

Santen Oy

Tél/Tel: +32 (0) 24019172

# България

Santen Oy

Тел.: +40 21 528 0290

# Česká republika

Santen Oy

Tel: +358 (0) 3 284 8111

### **Danmark**

Santen Oy

Tlf.: +45 898 713 35

#### **Deutschland**

Santen GmbH

Tel: +49 (0) 3030809610

# **Eesti**

Santen Oy

Tel: +372 5067559

### Ελλάδα

Santen Oy

Τηλ: +358 (0) 3 284 8111

### España

Santen Pharmaceutical Spain S.L.

Tel: +34 914 142 485

# France

Santen S.A.S.

Tél: +33 (0) 1 70 75 26 84

### Hrvatska

Santen Oy

Tel: +358 (0) 3 284 8111

### **Ireland**

Santen Oy

Tel: +353 (0) 16950008

# Ísland

Santen Oy

Sími: +358 (0) 3 284 8111

### Lietuva

Santen Oy

Tel: +370 37 366628

### Luxembourg/Luxemburg

Santen Oy

Tél/Tel: +352 (0) 27862006

### Magyarország

Santen Oy

Tel: +358 (0) 3 284 8111

### Malta

Santen Oy

Tel: +358 (0) 3 284 8111

### Nederland

Santen Oy

Tel: +31 (0) 207139206

# Norge

Santen Oy

Tlf: +47 21939612

# Österreich

Santen Oy

Tel: +43 (0) 720116199

### Polska

Santen Oy

Tel.: +48(0) 221042096

### **Portugal**

Santen Oy

Tel: +351 308 805 912

### România

Santen Oy

Tel: +358 (0) 3 284 8111

### Slovenija

Santen Oy

Tel: +358 (0) 3 284 8111

### Slovenská republika

Santen Oy

Tel: +358 (0) 3 284 8111

Italia

Santen Italy S.r.l.

Tel: +39 0236009983

Κύπρος

Santen Oy

Τηλ: +358 (0) 3 284 8111

Latvija

Santen Oy

Tel: +371 677 917 80

This leaflet was last revised in

Other sources of information

Santen Oy

Suomi/Finland

Puh/Tel: +358 (0) 974790211

**Sverige** Santen Oy

Tel: +46 (0) 850598833

Detailed information on this medicine is available on the European Medicines Agency web site: <a href="https://www.ema.europa.eu">https://www.ema.europa.eu</a>.